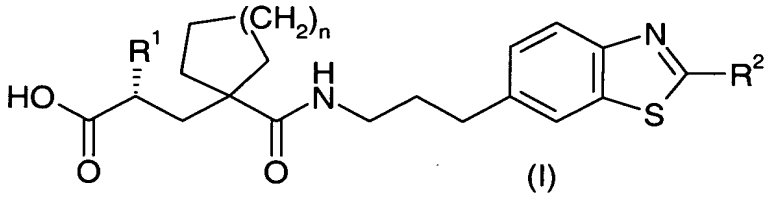
Claims

1. A compound of formula (I)



(I)

wherein:

R^1 is H or CH_3;

R^2 is C_1-C_2 alkyl; and

n is 1 or 2;

a tautomer thereof or a pharmaceutically acceptable salt, or solvate of said compound or tautomer.

2. The compound according to Claim 1 wherein n is 1.

3. The compound according to Claim 1 or Claim 2 wherein R^1 is hydrogen.

4. The compound according to Claim 3 wherein R^2 is methyl.

5. The compound according to Claim 3 wherein R^2 is ethyl.

6. The compound according Claim 1 or Claim 2 wherein R^1 is methyl.

7. The compound according to Claim 6 wherein R^2 is methyl.

8. The compound according to Claim 6 wherein R^2 is ethyl.

9. The compound according to Claims 1 or 2 wherein R^2 is methyl.

10. The compound according to Claims 1 or 2 wherein R^2 is ethyl.

11. The compound according to Claim 1 selected from

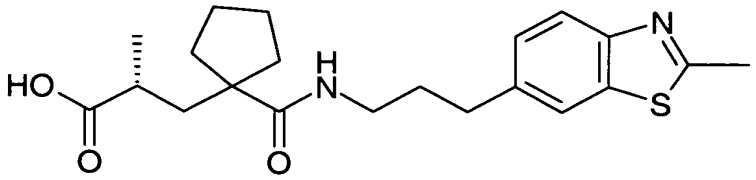
(*R*)-2-Methyl-3-(1-{[3-(2-methyl-1,3-benzothiazol-6-yl)propyl]carbamoyl} cyclopentyl)propanoic acid;

3-(1-{[3-(2-ethyl-1,3-benzothiazol-6-yl)propyl]carbamoyl}cyclopentyl)propanoic acid;

(*R*)-2-Methyl-3-(1-{[3-(2-ethyl-1,3-benzothiazol-6-yl)propyl]carbamoyl} cyclopentyl)propanoic acid; or

3-(1-{[3-(2-ethyl-1,3-benzothiazol-6-yl)propyl]carbamoyl}cyclohexyl)propanoic acid.

12. A compound of Formula Ia,



Ia,

a tautomer thereof or a pharmaceutically acceptable salt, or solvate of said compound or tautomer.

13. A pharmaceutical composition comprising a compound of formula (I) as claimed in any one of Claims 1, 2, 11 or 12, or pharmaceutically acceptable salts or solvates thereof, and a pharmaceutically acceptable diluent or carrier.

14. The pharmaceutical composition according to Claim 13 further comprising at least one of the following active ingredients: prostaglandins; α-adrenergic receptor antagonist compounds; NO-agonist compounds; potassium channel openers or modulators; dopaminergic agents; vasodilator agents; thromboxane A2 agonists; CNS active agonists; orgot alkoloids; modulators of natruretic factors; angiotensin-converting enzyme inhibitors; angiotensin receptor antagonists; substrates for NO-synthase; calcium channel blockers; endothelin receptor antagonists; endothelin-converting enzyme inhibitors; cholesterol-lowering agents; antiplatelet agents; antithrombotic agents; insulin sensitizing agents; L-DOPA; carbidopa; acetylcholinesterase inhibitors; steroidal anti-inflammatory agents; non-steroidal anti-inflammatory agents; estrogen receptor modulators; estrogen agonists and/or antagonists; cannabinoid receptor modulators; NPY inhibitors; vasoactive intestinal protein; melanocortin receptor agonist or modulator or enhancer; serotonin receptor agonists, antagonist or modulator; androgen; oestrogen; modulator of transporters for noradrenaline, dopamine and or serotonin; purinergic receptor agonist and/or modulator; neurokinin receptor antagonists; opioid receptor agonist, antagonist or modulator; oxytocin/vasopressin receptor agonists or modulator or PDE inhibitors.

15. A method of treating or preventing a disorder or condition by inhibiting NEP in a mammal, comprising administering to said mammal a therapeutically effective amount of a compound of formula (I) as claimed in any one of Claims 1, 2, 11 or 12, or a pharmaceutically acceptable salt, or solvate thereof.

16. The method according to Claim 15 wherein R^1 is hydrogen.

17. The method according to Claim 16 wherein R^2 is methyl.

18. The method according to Claim 16 wherein R^2 is ethyl.

19. The method according to Claim 15 wherein R^1 is methyl.

20. The method according to Claim 19 wherein R^2 is methyl.

21. The method according to Claim 20 wherein R^2 is ethyl.

22. The method according to Claim 15 wherein R^2 is methyl.

23. The method according to Claim 15 wherein R^2 is ethyl.

24. The method according to Claim 15, wherein the disorder or condition is selected from hypertension, essential hypertension, pulmonary hypertension, secondary hypertension, isolated systolic hypertension, hypertension associated with diabetes, hypertension associated with atherosclerosis, and renovascular hypertension, peripheral vascular disease, heart failure, angina, renal insufficiency, acute renal failure, cyclical oedema, Menières disease, hyperaldosteroneism (primary and secondary), hypercalciuria, stroke, glaucoma, obesity, metabolic diseases, Metabolic Syndrome, diabetes, impaired glucose tolerance, diabetic retinopathy, diabetic neuropathy, menstrual disorders, preterm labour, pre-eclampsia, endometriosis, and reproductive disorders, male and female infertility, polycystic ovarian syndrome, implantation failure, asthma, inflammation, leukemia, pain, cancer pain, depression, drug abuse, cirrhosis, epilepsy, affective disorders, dementia and geriatric confusion, gastrointestinal disorders, diarrhoea, irritable bowel syndrome, wound healing, diabetic and venous ulcers and pressure sores, septic shock, gastric acid secretion, hyperreninaemia, cystic fibrosis, restenosis, athereosclerosis, female sexual dysfunction (FSD), sexual arousal disorder, female sexual arousal disorder (FSAD), male sexual dysfunction (MSD), male erectile dysfunction (MED), hypoactive sexual desire disorder, orgasmic disorder and sexual pain disorder.

25. The method according to Claim 24 wherein the disorder or condition is selected from female sexual dysfunction (FSD), sexual arousal disorder, female sexual arousal disorder (FSAD), male sexual dysfunction (MSD), male erectile dysfunction (MED), hypoactive sexual desire disorder, orgasmic disorder and sexual pain disorder.

26. The method according to Claim 25 wherein the disorder or condition is selected from female sexual dysfunction (FSD), female sexual arousal disorder (FSAD), male sexual dysfunction (MSD), and male erectile dysfunction (MED).

27. A method of treating or preventing a disorder or condition by inhibiting NEP in a mammal, comprising administering to said mammal a therapeutically effective amount of the composition as claimed in Claim 14 or a pharmaceutically acceptable salt, or solvate thereof.

28. The method according to Claim 27 wherein the disorder or condition is selected from female sexual dysfunction (FSD), female sexual arousal disorder (FSAD), male sexual dysfunction (MSD), and male erectile dysfunction (MED).

29. The method according to Claim 28, wherein the disorder is FSD and the active ingredient is a

(a) PDE5 inhibitor selected from:

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one sildenafil;

(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylene-dioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione;

2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-1-sulphonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one;

5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; and

5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one

and pharmaceutically acceptable salts thereof;

(b) an NPY Y1 inhibitor;

(c) a dopamine agonist selected from apomorphine or a selective D_2, D_3 or D_2/D_3agonist selected from pramipexole and ropirinol;

(d) a melanocortin receptor agonist or modulator or melanocortin enhancer selected from melanotan II, PT-14, PT-141;

(e) an agonist, antagonist or modulator for 5HT2C;

(f) an estrogen receptor modulator, agonist and/or antagonists selected from raloxifene, tibolone or lasofoxifene;

(g) an androgen selected from androsterone, dehydro-androsterone, testosterone, androstanedione or a synthetic androgen; and

(h) an oestrogen selected from oestradiol, oestrone, oestriol or synthetic estrogen.

30. The method according to Claim 27 wherein the disorder is MED and the active ingredient is:

(a) a PDE5 inhibitor selected from:

5-[2-ethoxy-5-(4-methyl-1-piperazinylsulphonyl)phenyl]-1-methyl-3-n-propyl-1,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one sildenafil;

(6R,12aR)-2,3,6,7,12,12a-hexahydro-2-methyl-6-(3,4-methylene-dioxyphenyl)-pyrazino[2',1':6,1]pyrido[3,4-b]indole-1,4-dione;

2-[2-ethoxy-5-(4-ethyl-piperazin-1-yl-1-sulphonyl)-phenyl]-5-methyl-7-propyl-3H-imidazo[5,1-f][1,2,4]triazin-4-one;

5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; and

5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one
and pharmaceutically acceptable salts thereof;

(b) an NPY Y1 inhibitor;

(c) a dopamine agonist selected from apomorphine or a selective D_2, D_3 or D_2/D_3agonist selected from pramipexole and ropirinol;

(d) a melanocortin receptor agonist or modulator or melanocortin enhancer selected from melanotan II, PT-14, PT-141; or

(e) an agonist, antagonist or modulator for 5HT2C.

31. The method according to Claim 27 wherein the condition is a cardiovascular disorder and the active ingredient is:

(a) angiotensin receptor blockers selected from losartan, valsartan, telmisartan, candesartan, irbesartan, eprosartan or olmesartan;

(b) calcium channel blockers selected from amlodipine;

(c) statins selected from atorvastatin;

(d) PDE5 inhbitors selected from sildenafil, tadalafil, vardenafil, 5-[2-ethoxy-5-(4-ethylpiperazin-1-ylsulphonyl)pyridin-3-yl]-3-ethyl-2-[2-methoxyethyl]-2,6-dihydro-7H-pyrazolo[4,3-d]pyrimidin-7-one; 5-(5-acetyl-2-butoxy-3-pyridinyl)-3-ethyl-2-(1-ethyl-3-azetidinyl)-2,6-dihydro-7*H*-pyrazolo[4,3-*d*]pyrimidin-7-one; or N-[[3-(4,7-dihydro-1-methyl-7-oxo-3-propyl-1H-pyrazolo[4,3-d]-pyrimidin-5-yl)-4-propxyphenyl]sulfonyl]-1-methyl2-pyrrolidinepropanamide;

(e) beta blockers selected from atenolol or carvedilol

(f) ACE inhibitors selected from quinapril, enalapril or lisinopril;

(g) alpha-blockers selected from doxazosin;

(h) selective aldosterone receptor antagonists selected from eplerenone or spironolactone; or

(i) imidazoline I_1 agonists selected from rilmenidine or moxonidine.

32. The method according to Claims 27 wherein the composition is administered orally, bucally or sublingually and the therapeutically effective amount of the composition is 5 mg to 1000 mg.

33. The method according to Claim 32 wherein the composition is administered orally.